REMARKS

Please reconsider the present application in view of the above amendments and the following remarks. Applicant thanks the Examiner for carefully considering this application.

Disposition of Claims

Claims 1-10 are pending in the present application. Of these claims, claim 1 is independent. The remaining claims are, directly or indirectly, dependent from claim 1. The Applicant respectfully notes that Office Action Summary states claims 1-5 are pending in the application. However, new claims 6-10 have been added in the preliminary amendment filed September 29, 2005, and thus, claims 1-10 are now pending in this application.

Claim Amendments

By way of this reply, claim 1 has been amended to clarify the invention. Specifically, the further limitation *"continued for about 4 weeks"* has been added to the claim as the release period of HGF. No new matter has been added by way of the amendment. Support for the amendment may be found, for example, in paragraph [0065] of the published application.

Rejection(s) under 35 U.S.C. §112

Claims 4 and 5 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner asserts that the specification does not adequately teach HGF containing gels to be used to treat hypertrophic cardiomyopathy, idiopathy, primary cardiomyopathy, or cardiomyopathy as recited in claims 4 and 5. This rejection is respectfully traversed.

At the outset, the specification of the present application specifically teaches *"the applicable disease of an HGF gradual release gelatin hydrogel preparation of the present invention is cardiomyopathy,"* and *"Cardiomyopathy as referred to in the present invention refers to all diseases for which lesions are observed in heart muscle that are characterized by the absence of a well-defined cause and abnormal hypertrophy, degeneration or fibrosis of heart muscle."*(*see,* paragraph [0050] of the published application).

Further, for example, Nippon Rinsho, 59, 2460-2469, issued 2001 ("Aoki *et al.*"), which is titled "HGF as a key molecule in cardiovascular diseases," specifically teaches that HGF is able to suppress the fibrosis of myocardium in hepatic cirrhosis model.

Therefore, it is clear for one skilled in the art that the HGF containing gels of the present invention can be used to treat hypertrophic cardiomyopathy, idiopathy, primary cardiomyopathy, or secondary cardiomyopathy, recited in claims 4 and 5.

Thus, as those skilled in the art at the time of the invention in possession of the present specification would be readily able to make and use the invention described in the present specification, claims 4 and 5 are fully supported and enabled by the original specification. In view of the above, claims 4 and 5 meet the requirements of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection(s) under 35 U.S.C. § 102

Claims 1-5 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Circulation, 106, supplement, p II-350, Nov., 2002, Meeting abstract ("Tambara"). By way of this reply, independent claim 1 has been amended to clarify the invention. To the extent that this

rejection may still apply to amended independent claim 1, the rejection is respectfully traversed for the reasons set forth below.

Applicant respectfully notes that MPEP § 2131 makes it clear that a claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently in a single prior art reference. Of the rejected claims, amended claim 1 is independent, and includes, in part, a limitation of "*gradually releases HGF continued for about 4 weeks.*"

One or more embodiment in the present invention is directed to cardiomyopathy therapeutic agent containing hepatocyte growth factor (HGF) and gelatin hydrogel, and gradually releasing the HGF. As a result of conducting extensive studies on therapeutic agents for dilated cardiomyopathy, the inventors of the present invention found that a cardiomyopathy therapeutic agent containing HGF and gelatin hydrogel, gradually releases the HGF continued for a long period. An experimental result in the application demonstrates the gradual release of HGF from the agent continues for 4 weeks, and aggressive therapeutic effects continue for the same period (see, paragraphs [0058]-[0065] in the published application). Accordingly, the claimed invention includes, in part, a limitation of "*gradually releases HGF continued for about 4 weeks.*"

In contrast, Tambara discloses a controlled release of HGF via gelatin hydrogel sheets. However, the gelatin hydrogel in Tambara is capable of releasing HGF for only two weeks, because the gelatin hydrogel in Tambara is prepared by chemically bridging the gelatin as a matrix, and in this case, degradation time of the gelatin hydrogel is dependent on the level of chemical bridge.

Accordingly, Tambara does not disclose or suggest at least "*gradually releases HGF continued for about 4 weeks*" as recited in claim 1. Thus, independent claim 1 is patentable over Tambara. Dependent claims 2-10 are also patentable for at least the same reasons. Therefore, withdrawal of this rejection is respectfully requested.

Rejection(s) under 35 U.S.C. § 103

Claims 1-5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over European Patent Application Publication 0,702,959 ("Tabata") in view of U.S. Patent No. 5,362,716 ("Kmiecik"). By way of this reply, independent claim 1 has been amended to clarify the invention. To the extent that this rejection may still apply to amended independent claim 1, the rejection is respectfully traversed for the reasons set forth below.

As discussed above, one or more embodiment in the present invention is directed to cardiomyopathy therapeutic agent containing hepatocyte growth factor (HGF) and gelatin hydrogel, and gradually releasing the HGF continued for 4 weeks. Thus, aggressive therapeutic effects of the present invention continue for the same period. Accordingly, the claimed invention includes, in part, limitations of *"cardiomyopathy therapeutic agent containing HGF"* and "*gradually releases HGF continued for about 4 weeks*." In contrast, as the Examiner acknowledged, Tabata teaches various cross-linked gelatin preparations with methods, but does not teach or suggest the use of HGF in gelatin. However, the Examiner asserts that Kmiecik shows the use of HGF in gels (*see,* on page 6 of the Office Action).

At the outset, Applicant respectfully notes that Tabata and Kmiecik are both non-analogous arts to the present invention, and accordingly, it is improper to apply either Tabata or Kmiecik against the pending claims.

As discussed above, the claimed invention is directed to cardiomyopathy therapeutic agent containing hepatocyte growth factor (HGF). In contrast, Tabata is directed to a cross-linked gelatin gel preparation containing a basic fibroblast growth factor (bFGF), which stimulates the proliferation of fibroblast. The disclosure of Tabata is not at all related to cardiomyopathy therapeutic effects. Further, the particular problem with which the present inventors were faced is to select and optimize gelatin condition such as acidic gelatin, alkaline gelatin, cationic gelatin, anionic gelatin, hydrophobic gelatin, hydrophilic gelatin, and rate of incorporation, for preparing *"cardiomyopathy therapeutic agent containing hepatocyte growth factor (HGF) and gelatin hydrogel, and gradually releasing the HGF."* Moreover, interactions between gelatin and an agent to be incorporated are widely varied depending on the agent's properties, such as isoelectric point, molecular weight, ratio of hydrophobic and hydrophilic group, steric barrier by its conformation, state of molecular surface, and the like. In other words, the particular problems faced for selecting or optimizing a gelatin hydrogel composition containing bFGF is distinguished from the particular problems faced for selecting or optimizing a gelatin hydrogel composition containing HGF. Accordingly, Tabata is (1) not in the same field of endeavor as the present invention and (2) not pertinent to the particular problem with which the present inventors were faced (*see,* MPEP 2141.01(a)). Accordingly, Tabata is non-analogous art to the present application and the application of Tabata against the pending claims is improper.

Further, Kmiecik is directed to utilizing a complex of HGF and its receptor to regulate the intrinsic tyrosine kinase activity. In Kmiecik, the effect of HGF on the growth of cells was examined in soft agar colony assays. As discussed above, the claimed invention is directed to cardiomyopathy therapeutic agent containing hepatocyte growth factor (HGF) and gelatin hydrogel, and gradually releasing the HGF continued over a long period. In contrast,

there exists nothing whatsoever in the disclosure of Kmiecik about gradual release of HGF from a specific substrate that even recognizes, much less addresses, such a problem. Further, agar is a polysaccharide obtained from seaweed, and thus, is a substantially different material from gelatin, which is a protein obtained from an animal. Accordingly, Kmiecik is (a) not in the same field of endeavor as the present invention and (b) not pertinent to the particular problem with which the present inventors were faced (*see,* MPEP 2141.01(a)). Accordingly, Kmiecik is non-analogous art to the present application and the application of Kmiecik against the pending claims is improper.

Furthermore, even assuming, *arguendo,* that each reference is properly applied, there is no suggestion or motivation, and, in fact, there would be no reasonable expectation of success, in combining the references. To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 706.02(j). First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

In the present case, neither Tabata, nor Kmiecik, impliedly or expressly provide any motivation to combine their respective teachings to achieve the claimed invention. As discussed above, Tabata is directed solely to selecting or optimizing a gelatin hydrogel composition containing bFGF. Meanwhile, Kmiecik is solely directed to utilizing a complex of

HGF and its receptor to regulate the intrinsic tyrosine kinase activity, and uses only soft agar for examining the effect of HGF on the growth of cells. Agar is a polysaccharide obtained from seaweed, and thus, is a substantially different material from gelatin, which is a protein obtained from an animal. Therefore, there exists nothing in either of the unrelated disclosures of Tabata and Kmiecik that would motivate one skilled in the art to combine their teachings in an attempt to provide the claimed *cardiomyopathy therapeutic agent containing hepatocyte growth factor (HGF) and gelatin hydrogel, and gradually releasing the HGF for about 4 weeks.* Moreover, in view of the unpredictability of the chemical arts, in particular, in this case, the widely varying interactions between gelatin and an agent to be incorporated, together with the significant differences between the teachings of Tabata, the teaching of Kmiecik, and the claimed invention, one skilled in the art has no reasonable expectation of success in combining the unrelated teachings of Tabata and Kmiecik in an attempt to achieve the claimed invention.

In view of the above, independent claim 1 is patentable over Tabata and Kmiecik because (1) both references are non-analogous art to the present application and the application of the references against the pending claims are improper, and (2) neither Tabata, nor Kmiecik providing any motivation or suggestion, and, in fact, there is no reasonable expectation of success, to combine the teaching of Tabata and Kmiecik in an attempt to provide the claimed invention. Dependent claims are allowable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

Double Patenting

Claims 1 and 2 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting. An appropriate terminal disclaimer is filed herewith. Accordingly, thid rejection is now moot.

Conclusion

Applicant believes this reply is fully responsive to all outstanding issues and places this application in condition for allowance. If this belief is incorrect, or other issues arise, the Examiner is encouraged to contact the undersigned or his associates at the telephone number listed below. Please apply any charges not covered, or any credits, to Deposit Account 50-0591 (Reference Number 17195/006001).

Dated: 7/30/07

Respectfully submitted,

By #45,079
Jonathan P. Osha THOMAS SCHERER
Registration No.: 33,986
OSHA · LIANG LLP
1221 McKinney St., Suite 2800
Houston, Texas 77010
(713) 228-8600
(713) 228-8778 (Fax)
Attorney for Applicant